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BRCA1/2 Testing in Hereditary Breast and Ovarian Cancer Families II: Impact on Relationships

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Members of hereditary breast and ovarian cancer (HBOC) families often express concern during genetic counseling about the impact of BRCA1/2 testing on close relatives. Yet whether there are likely to be adverse effects of either the decision to undergo genetic testing or the results of testing on family relationships is unknown. One purpose of this study was to assess the impact on close family relationships. Within a randomized trial of breast cancer genetic counseling methods, members of 13 HBOC families were offered BRCA1/2 testing for a known family mutation. The Family Relationship Index (FRI) of the Family Environment Scale (FES) was used to measure perceived family cohesion, conflict, and expressiveness at baseline and again 6–9 months following the receipt of test results, or at the equivalent time for those who declined testing. Participants (n = 212) completed baseline and follow-up questionnaires. Comparisons were made between testers and non-testers as well as between those who tested positive and negative for the family mutation. One hundred eighty-one participants elected to undergo genetic testing (85%) and 47 (26%) were identified to have a mutation. After adjusting for baseline family relationship scores, counseling intervention, gender and marital status, non-testers reported a greater increase in expressiveness ($P = 0.006$) and cohesion ($P = 0.04$) than testers. Individuals who tested positive reported a decrease in expressiveness ($P = 0.07$), although as a trend. Regardless of test decision or test result, those who were randomized to a client-centered counseling intervention reported a decrease in conflict ($P = 0.006$). Overall, study results suggest that undergoing genetic testing and learning ones BRCA1/2 status may affect family relationships. Those individuals who declined testing reported feeling closer to family members and more encouraged to express emotions to other family members demonstrating potential benefit from the offer of testing. Since those who tested positive reported feeling less encouraged to express their emotions within the family, we recommend helping clients to identify others with whom they feel comfortable sharing their thoughts and feelings about their positive gene status and increased cancer risk. **Published 2005 Wiley-Liss, Inc.†**

KEY WORDS: family cohesion; conflict; expressiveness; genetic counseling; cancer risk testing

INTRODUCTION

It is estimated that 213,910 American women will be diagnosed with breast cancer in 2004 [American Cancer Society, 2003]. These women will have to deal with the trauma of diagnosis, treatment, the fear of dying and, as treatment is increasingly successful, the reality of surviving cancer and living with the risk of recurrence. The success with which they adjust depends on many factors, such as their personality [Roberts et al., 1994], demographics [Bloom, 1982], religious beliefs [Carey, 1974], stage of disease, and type of treatment [Meyerowitz, 1980]. Importantly, one of the greatest predictors of adjustment has been shown to be social support, particularly emotional support [Bloom, 1982; Bloom and Spiegel, 1984; Neuling and Winefield, 1988; Kaye and Gracely, 1993]. Not only does breast cancer have an impact on the individual, it also affects the family members who offer this needed support, and consequently family relationships and dynamics. While it is clear that cancer itself has an impact on family members and family dynamics, it is less clear to what extent, if any, shared risk for cancer and more specifically, genetic testing for hereditary cancer predisposition, may adversely affect family relationships.

Impact of Genetic Testing for Cancer on Families

Family relationships are important sources of social support and in turn a strong predictor of adjustment for patients with many illnesses including cancer [Bloom, 1982; Holahan and Moos, 1982]. Women who perceive their families to be highly cohesive have been shown to have better coping responses and adjustment in all three areas: self-concept, sense of power, and psychological distress [Bloom, 1982]. Most of the studies of genetic testing in hereditary breast and ovarian cancer (HBOC) families to date have focused on the communication

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of genetic test results within the family rather than on family relationships. Hughes et al. [2002] assessed the communication of BRCA1/2 test results to relatives of 43 women who had undergone testing. Although relaying genetic information was the primary reported reason for communicating results, carriers also reported wanting to share this information to gain emotional support or advice about medical decisions. Studying the communication of results from parents to children revealed that mothers and parents with higher levels of baseline distress were significantly more likely to communicate their test results to their children [Tercyak et al., 2001]. Interestingly, this action did not minimize the disclosers' distress and, was conjectured to lead to distress in their children.

As one might predict, psychological well-being may be influenced not only by one's own genetic test results but also by the results of one's siblings. It has been suggested that the joy of a good news result for oneself might be tainted by pain in learning that a sibling received a bad news result [Biesecker et al., 1993; Smith et al., 1999]. Smith et al. [1999] measured distress in 212 members of large BRCA1 kindred prior to testing and 1–2 weeks after receiving results. They found that non-carrier males whose siblings all tested positive encountered significant test-related distress, which was interpreted to be the result of survivor guilt. They also found that distress was highest in women who tested positive whose siblings all tested negative. When some or all siblings had positive results, mutation positive women seemed to cope better. Hamann et al. [2003] assessed perceived warmth and dominance in sibling support among 49 pairs of siblings receiving BRCA1/2 results. Dyads who received identical results, either positive or negative, reported more positive sibling behaviors than those who received discordant results. These findings demonstrate that genetic test results can affect family relationships. However, it is unlikely that these effects capture the full impact on family relationships or whether they are sustained over time.

Hypotheses

For this analysis, we hypothesized that;

choosing not to undergo testing will have more adverse effects on family relationships than undergoing testing;
a positive test result will more often lead to a decrease in expressiveness, increase in conflict, and decrease in cohesion;
those participants with a personal history of cancer will have fewer changes in family relationships as a result of genetic testing; and
the counseling model used, marital status and gender will moderate changes in family relationships.

METHODS

Study Population

Five hundred fifty nine letters of invitation were sent to all eligible adult (>18 years old) men and women from 13 extended HBOC families in which BRCA1/2 mutations had been identified. There were 262 individuals who agreed to participate and completed the baseline questionnaire. Data from the 212 (81%) individuals who completed both the baseline and follow-up questionnaires were analyzed.

Study Protocol

Prior to education and counseling participants completed a baseline questionnaire that included the Family Environment Scale (FES). A standardized group (family) education session was followed by an hour-long individual counseling session. Participants were randomized to receive either a client-centered counseling session or a counselor-driven problem solving counseling session. All participants were contacted 6–9 months after results were given, or would have been given, to participate in a telephone interview that included administering the FES a second time.

All education, counseling, and testing were provided under an intramural NIH research protocol (95-HG-0085) that was approved by the NCI Institutional Review Board.

Intervention

We have published elsewhere [McInerney-Leo et al., 2004] a detailed description of the counseling interventions used in this study. Client-centered counseling had a less structured format that followed the client's feelings and thoughts about their test decision. Problem-solving training was structured to focus on one aspect of testing that was of greatest concern to the client along with identification of potential solutions and their likely consequences.

Measures

Sociodemographics. Participant data on gender, age, education, employment status, income category, religious affiliation, marital status, and cancer history were gathered.

Psychosocial variables. Dimensions of family relationships including conflict, cohesiveness, and expressiveness were measured using the Family Relationship Index (FRI), a subscale of the FES. The FES is a 90-item survey on self-perception of the nuclear family environment and participants were asked to complete the questionnaire with immediate family relationships in mind. It has been found to have moderate to high internal consistencies (ranging from 0.61 to 0.78) and acceptable test–retest reliabilities (0.68–0.86) in numerous studies [Holahan and Moos, 1982]. The FRI has been found to have good construct validity as an index of social support in terms of its relationship to other measures of social support and to outcome indices [Holahan and Moos, 1982]. The Cohesion subscale measures the degree of commitment, help, and support family members provide to one another while the Expressiveness subscale captures the extent to which family members are encouraged to act openly and to express their feelings directly. The Conflict subscale ascertains the amount of openly expressed anger, aggression, and conflict among family members [Moos and Moos, 1994]. Participants were asked to complete the scale keeping in mind their relationships with their closest relatives.

Statistical Analysis

Paired t-tests and ANOVAs were used to assess associations between the sociodemographic variables and any change in psychosocial variables. Linear regression was used to model the 6–9 months follow-up family relationship scores as a function of the baseline family relationship scores, test results (or testing status), gender, marital status, cancer history, and intervention group. One model examined differences between testers versus non-testers and the other model examined differences between those who tested positive versus those who tested negative. Robust standard errors were used to take into account the possible correlation of subjects within family. Interpretation of statistical significance was based on a $P \leq 0.05$. Analyses were performed using STATA (version 7).

RESULTS

Two hundred sixty two individuals completed the baseline questionnaire and were offered genetic testing after education and counseling. Two hundred and twelve of these were assessed at both baseline and 6–9 months follow-up. There were no

statistical differences in sociodemographics, cancer history, and testing decision/results between those who only completed the baseline questionnaire and those who completed both baseline and follow-up questionnaires. Participants were primarily Caucasian and well-educated. Over half were over the age of 40 and 65% were female. Eighty-five percent chose to be tested and 26% of testers had the familial mutation. A more detailed population description is published elsewhere [McInerney-Leo et al., 2004].

Bivariate Analysis

Table I summarizes the data on family relationship scores at baseline and at 6–9 months follow-up for those participants with a positive test result, a negative test result, and for those participants who did not elect to undergo the genetic testing. Perceptions of family cohesion increased significantly for testers ($P = 0.047$) but the increase from baseline was highly significant in those who chose not to undergo testing ($P < 0.001$). While expressiveness did not change significantly in both those who tested negative and those who chose not to have testing, it decreased significantly in those who tested positive ($P = 0.003$). Conflict decreased from baseline for those who underwent testing ($P = 0.05$).

Multivariate Analysis

Tables II and III include the estimated change in family relationship scores upon comparing testers to non-testers, and those who tested positive to those who tested negative, adjusting for baseline family relationship scores, intervention, gender, and marital status. Non-testers were found to have significantly greater increases in expressiveness ($P = 0.006$) and in cohesion ($P = 0.04$) than testers. Although those who tested positive for BRCA1/2 mutation had a greater reduction in their follow-up expressiveness score compared to those who tested negative, after adjusting for baseline expressiveness score, intervention, gender, and marital status the difference was no longer significant ($P = 0.07$). Regardless of test decision, clients randomized to the client-centered intervention had significantly greater reduction in conflict as compared to those randomized to problem solving training ($P = 0.006$).

DISCUSSION

This study evaluated perceived changes in family relationships as a result of the offer of BRCA1/2 testing or receipt of the results. This prospective study provided the opportunity to examine our hypotheses about the impact on relationships within HBOC families.

Testers Versus Non-Testers

We hypothesized that being presented with the option of testing but choosing not to be tested would increase psychological distress and therefore expected that choosing not to undergo testing may have more adverse effects on relationships among relatives than choosing to undergo testing. This hypothesis was supported by results from a study that assessed psychological well-being 6 months post testing and found that decliners had an increase in depressive symptoms [Lerman et al., 1998]. Contrary to our hypothesis, non-testers reported positive changes in family relationships, particularly in expressiveness and cohesion when compared to those who chose testing. This finding suggests that members of some HBOC families, those choosing not to undergo genetic testing, feel encouraged by close relatives to express their feelings and supported by them to a greater extent during the months following the offer of genetic testing. There have been conflicting results about whether individuals experience psychological distress following the decision not to undergo cancer genetic testing [Lerman et al., 1998; McInerney-Leo et al., 2004], however, our findings suggest certain families may find benefits in making a decision about testing, even when they decline it. Whether these are sustained perceptions cannot be addressed by our results as our follow-up data was collected only 6–9 months following receipt of test results or during the equivalent time for non-testers.

Positive Versus Negative Test Results

Clinical experience led us also to hypothesize that a positive test result was more likely to lead to decrease in expressiveness, increase in conflict, and decrease in cohesion. There was only a trend toward a decrease in expressiveness among those who tested positive in comparison to those who tested negative, though those who tested positive were still in the average range of normal.

Compared with those who received a negative result, those who received a positive test result seemed to feel that there was less encouragement from their close relatives to express their feelings. It may be that a positive test result inhibited communication with relatives who received negative test results. Conversely, the lessening of expressiveness in those who tested positive may represent a way of coping. When Tercyak et al. [2001] evaluated parental communication of BRCA1/2 test results to children, their findings indicated that parents who chose to share positive test results with their children did not minimize their psychological distress by doing so. A trend toward reduction in expressiveness within families 6–9 months after testing may reflect an initial tendency to discuss emotions

TABLE I. Mean and Standard Deviation of Family Relationship Scores Comparing Baseline and 6–9 Months Follow-Up

Family Relationship Index (FRI)	Outcome	Baseline	6–9 months follow-up	*P*
Cohesion	Positive test	7.48 (1.99)	7.70 (2.06)	0.379
	Negative test[a]	7.82 (1.49)	8.04 (1.59)	0.073
	Testers	7.73 (1.63)	7.95 (1.72)	0.047
	Non-tester	6.79 (2.65)	8.00 (1.75)	<0.001
Expressiveness	Positive test	6.30 (1.92)	5.50 (2.14)	0.003
	Negative test[a]	6.09 (2.03)	6.12 (2.22)	0.842
	Testers	6.15 (2.00)	5.96 (2.21)	0.166
	Non-tester	6.00 (2.34)	6.39 (2.08)	0.133
Conflict	Positive test	2.05 (1.98)	1.79 (1.99)	0.259
	Negative test[a]	1.86 (1.64)	1.64 (1.80)	0.107
	Testers	1.90 (1.73)	1.67 (1.85)	0.050
	Non-tester	2.00 (1.98)	1.66 (1.86)	0.115

[a]Negative results in this study were "true" negatives.

TABLE II. Regression Analysis Comparing Change in Family Relationship Measures for all Study Participants (n = 212)

Outcome	Variables	Levels	Beta	*P*	Adj. R^2
Cohesion	Baseline coh		0.60 (0.06)	<0.001	0.379
At 6–9 months	Gender	Female	0.20 (0.23)	0.397	
	Marital status	Married	−0.06 (0.23)	0.790	
	Cancer history	Yes	0.01 (0.22)	0.981	
	Intervention	Client-centered	−0.24 (0.20)	0.258	
	Testing[a]	Yes	−0.58 (0.25)	0.040	
Expressiveness	Baseline express		0.69 (0.05)	<0.001	0.421
At 6–9 months	Gender	Female	0.26 (0.28)	0.368	
	Marital status	Married	0.25 (0.30)	0.425	
	Cancer history	Yes	−0.58 (0.58)	0.340	
	Intervention	Client-centered	−0.12 (0.27)	0.656	
	Testing	Yes	−0.56 (0.17)	0.006	
Conflict	Baseline conflict		0.71 (0.07)	<0.001	0.432
At 6–9 months	Gender	Female	−0.08 (0.13)	0.566	
	Marital status	Married	−0.19 (0.34)	0.602	
	Cancer history	Yes	−0.32 (0.26)	0.237	
	Intervention	Client-centered	−0.24 (0.08)	0.013	
	Testing	Yes	0.15 (0.29)	0.599	

[a]For example, participants who chose testing had an adjusted 6–9 months cohesion score 0.58 U lower than those who chose not to undergo testing ($P = 0.040$).

with individuals outside the family and this may have been a healthy choice for the psychological well-being of the relatives. This pattern of withholding thoughts or feelings which may be anxiety provoking for family members has been called protective buffering and has been reported in couples where one partner has been affected with cancer or suffered a myocardial infarction [Hagedoorn et al., 2000; Stewart et al., 2000]. More research is necessary to explore whether there is indeed a preference to discuss this information with individuals from outside the family and whether, given more time to adjust to the result, individuals feel more encouragement and willingness to express their emotions within the family.

Above average levels of cohesion were reported in this population at baseline [Biesecker et al., 2000]. There were no significant changes in cohesion levels in those who tested positive or in those who tested negative. This suggests that individuals who received a positive test result felt as closely connected to their family members as those who received a negative result. This is an important finding as higher levels of family cohesion scores have been strongly associated with healthy adjustment to stressful life events [Bloom, 1982]. Our findings suggest that individuals from cohesive families may be more likely to choose genetic testing, and this high level of cohesion may in turn make them more resilient to the impact of test results.

There was no significant change in conflict over time or related to test results. This suggests that there was no difference in the degree of openly expressed anger and conflict among families. If we were to see survivor guilt in this population as has been suggested in other HBOC families [Smith et al., 1999], we might expect those who tested negative to have had higher levels of conflict, based on feelings of guilt that could be manifested as hostility and resentfulness similar to what has been reported in non-carrier members of Huntington disease families [Meissen et al., 1988; Craufurd et al., 1989]. What is remarkable about conflict in this population is its absence. Baseline levels were below or well below average [Moos and Moos, 1994] and at follow-up these levels had only decreased further. If participants did harbor negative feelings about genetic testing we found no evidence that they externalized them or displaced their anger onto close relatives. It is also possible that, as in the case of cohesion, individuals from families with less conflict were more likely to participate in research and to choose to undergo genetic testing.

TABLE III. Regression Analysis Comparing Change in Family Relationship Measures for Those who Underwent Testing (n = 181)

Outcome	Variables	Levels	Beta	*P*	Adj. R^2
Cohesion	Baseline coh		0.62 (0.09)	<0.001	0.343
At 6–9 months	Gender	Female	0.13 (0.20)	0.532	
	Marital status	Married	0.04 (0.26)	0.873	
	Cancer history	Yes	0.28 (0.29)	0.363	
	Intervention	Client-centered	−0.24 (0.20)	0.249	
	Result	Positive	−0.25 (0.31)	0.433	
Expressiveness	Baseline express		0.68 (0.06)	<0.001	0.421
At 6–9 months	Gender	Female	0.42 (0.37)	0.279	
	Marital status	Married	0.23 (0.35)	0.532	
	Cancer history	Yes	−0.38 (0.75)	0.623	
	Intervention	Client-centered	0.09 (0.30)	0.763	
	Result	Positive	−0.66 (0.33)	0.070	
Conflict	Baseline conflict		0.71 (0.08)	<0.001	0.432
At 6–9 months	Gender	Female	−0.20 (0.16)	0.230	
	Marital status	Married	−0.28 (0.38)	0.473	
	Cancer history	Yes	−0.47 (0.34)	0.196	
	Intervention	Client-centered	−0.35 (0.10)	0.006	
	Result	Positive	0.13 (0.24)	0.583	

Gender, Marital Status, and Cancer History

As can be seen in Table II, the participants' gender, marital status, and cancer history do not appear to have any significant effects on change in family relationships regardless of testing decision or outcome. We hypothesized that cancer history would have a moderating role but it did not. Although these factors were not associated with changes in family relationships in these families, cancer history, gender, and marital status have been associated with changes in psychological well-being in this study and in others [Croyle et al., 1997; Lerman et al., 1998; McInerney-Leo et al., 2004].

Counseling Model

We further hypothesized that the counseling model to which participants were randomized would moderate changes to family relationships whether participants opted for testing or not. Individuals randomized to receive client-centered counseling had greater reductions in conflict than those who received problem solving training (Tables II and III). The client-centered sessions were much less structured and depended on the clients' concerns about testing. We conjecture that these sessions may have focused, more often than the problem solving sessions, on the potential for conflict among relatives thereby ultimately moderating it. Additional research is needed to investigate the long- and short-term outcomes of different cancer education and counseling models on family relationships.

STUDY LIMITATIONS

There were several limitations to our study. The findings are not generalizable to all HBOC families who may benefit from BRCA1/2 testing. There were selection biases, only some of which we can predict. Families in this study had previously participated in a large genetic linkage study that involved a need for communication among relatives. In addition, participants reported above average levels of family cohesion and below average levels of conflict. Further, not every member of each family agreed to participate.

SUMMARY

Overall, these findings serve as a preliminary step in elucidating the effects of BRCA1/2 testing on family relationships in HBOC families. Contrary to our hypothesis, declining testing did not appear to be associated with any negative impact on family relationships and was actually associated with an increase in family support and encouragement to express emotions. Family members who received a positive test result were somewhat more likely to experience decreased expressiveness 6–9 months after receiving their test results, as compared to those who received a negative test result. Our results suggest that counseling interventions can modify conflict within family relationships. How widespread this general lack of adversity is surrounding genetic testing among HBOC families remains to be studied.

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